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Search Results - Record(s) 1 through 7 of 7 returned.

☐ 1. Document ID: US 6072047 A

L1: Entry 1 of 7 File: USPT Jun 6, 2000

US-PAT-NO: 6072047
DOCUMENT-IDENTIFIER: US 6072047 A

TITLE: Receptor that binds trail

DATE-ISSUED: June 6, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rauch; Charles	Bainbridge Island	WA	N/A	N/A
Walczak; Henning	Seattle	WA	N/A	N/A

US-CL-CURRENT: 536/23.5; 435/252.3, 435/320.1, 435/325, 435/6, 435/69.1, 530/350, 536/24.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: WO 9903992 A1

L1: Entry 2 of 7 File: EPAB Jan 28, 1999

PUB-NO: WO009903992A1
DOCUMENT-IDENTIFIER: WO 9903992 A1
TITLE: TRAIL RECEPTOR

PUBN-DATE: January 28, 1999

INVENTOR-INFORMATION:

NAME	COUNTRY
DEGLI-ESPOSTI, MARIAPIA	N/A

INT-CL (IPC): C12N 15/12; C12N 15/62; C07K 14/715; C07K 16/28; C07K 16/46; A61K 38/17
EUR-CL (EPC): C07K014/705

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: WO 9835986 A1

L1: Entry 3 of 7 File: EPAB Aug 20, 1998

PUB-NO: WO009835986A1
DOCUMENT-IDENTIFIER: WO 9835986 A1
TITLE: RECEPTOR THAT BINDS TRAIL

PUBN-DATE: August 20, 1998

INVENTOR-INFORMATION:

NAME	COUNTRY
RAUCH, CHARLES	N/A
WALCZAK, HENNING	N/A

INT-CL (IPC): C07K 14/435; C07K 14/715; C07K 16/28; C12N 15/12; C12N 15/19
EUR-CL (EPC): C07K014/705; C07K014/715

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 4. Document ID: EP 1012179 A2, WO 9912963 A2, AU 9893863 A

L1: Entry 4 of 7 File: DWPI Jun 28, 2000

DERWENT-ACC-NO: 1999-276942
DERWENT-WEEK: 200035
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TITLE: Novel tumor necrosis factor receptor proteins TRAIL-R2 and TRAIL-R3

INVENTOR: TSCHOPP, J

PRIORITY-DATA: 1998US-0084422 (May 6, 1998), 1997US-0058631 (September 12, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1012179 A2	June 28, 2000	E	000	C07K014/00
WO 9912963 A2	March 18, 1999	E	028	C07K014/00
AU 9893863 A	March 29, 1999	N/A	000	C07K014/00

INT-CL (IPC): C07K 14/00

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Desc | Image

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☐ 5. Document ID: EP 998561 A1, WO 9903992 A1, AU 9883957 A

L1: Entry 5 of 7 File: DWPI May 10, 2000

DERWENT-ACC-NO: 1999-132236
DERWENT-WEEK: 200027

TITLE: New isolated TRAIL receptor polypeptides - used to develop products for treating e.g. thrombotic microangiopathy, multiple sclerosis, systemic lupus erythematosus or HIV infection

INVENTOR: DEGLI-ESPOSTI, M

PRIORITY-DATA: 1997US-0892119 (July 15, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 998561 A1	May 10, 2000	E	000	C12N015/12
WO 9903992 A1	January 28, 1999	E	050	C12N015/12
AU 9883957 A	February 10, 1999	N/A	000	C12N015/12

INT-CL (IPC): A61K 38/17; C07K 14/715; C07K 16/28; C07K 16/46; C12N 15/12; C12N 15/62

☐ 6. Document ID: MX 9907234 A1, WO 9835986 A1, AU 9866505 A, EP 1005488 A1, US 6072047 A, NZ 336929 A

L1: Entry 6 of 7 File: DWPI Jan 1, 2000

DERWENT-ACC-NO: 1998-480767
DERWENT-WEEK: 200115

TITLE: New TRAIL receptor protein and related oligomers, nucleic acid, vectors - used to inhibit TRAIL activity, e.g. in cases of thrombocytic purpura, clotting in small blood vessels etc., also for diagnosis

INVENTOR: RAUCH, C; WALCZAK, H

PRIORITY-DATA: 1997US-0883036 (June 26, 1997), 1997US-0799861 (February 13, 1997), 1997US-0815255 (March 12, 1997), 1997US-0829536 (March 28, 1997), 1997US-0869852 (June 4, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
MX 9907234 A1	January 1, 2000	N/A	000	C07K014/435
WO 9835986 A1	August 20, 1998	E	056	C07K014/435
AU 9866505 A	September 8, 1998	N/A	000	C07K014/435
EP 1005488 A1	June 7, 2000	E	000	C07K014/435
US 6072047 A	June 6, 2000	N/A	000	C07H021/04
NZ 336929 A	November 24, 2000	N/A	000	C07K016/28

INT-CL (IPC): C07H 21/04; C07K 14/435; C07K 14/715; C07K 16/28; C12N 15/12; C12N 15/19; C12N 15/63

☐ 7. Document ID: JP 2001505060 W, WO 9830693 A2, AU 9862386 A, EP 990031 A2, CN 1247567 A

L1: Entry 7 of 7 File: DWPI Apr 17, 2001

DERWENT-ACC-NO: 1998-399141
DERWENT-WEEK: 200128

TITLE: Human TRAIL receptor without an intracellular domain polypeptide - used in the diagnosis of immune system-related disorder(s)

INVENTOR: EBNER, R; FENG, P ; GENTZ, R L ; NI, J ; RUBEN, S M ; WEI, Y ; YU, G

PRIORITY-DATA: 1997US-0054885 (August 7, 1997), 1997US-0035496 (January 14, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 2001505060 W	April 17, 2001	N/A	150	C12N015/09
WO 9830693 A2	July 16, 1998	E	091	C12N015/12
AU 9862386 A	August 3, 1998	N/A	000	C12N015/12
EP 990031 A2	April 5, 2000	E	000	C12N015/12
CN 1247567 A	March 15, 2000	N/A	000	C12N015/12

INT-CL (IPC): A61K 38/00; A61K 38/17; A61K 39/395; A61K 45/00; A61P 1/16; A61P 7/00; A61P 9/10; A61P 19/08; A61P 25/16; A61P 25/28; A61P 31/12; A61P 35/00; A61P 37/00; A61P 37/06; A61P 43/00; C07K 14/705; C07K 14/715; C07K 16/28; C12N 1/21; C12N 5/10; C12N 15/09; C12N 15/12; C12N 15/63; C12N 15/70; C12N 15/85; C12N 15/86; C12P 21/02; C12P 21/08

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Search Results -

Term	Documents
TNF-RELATED.DWPI,EPAB,JPAB,USPT,PGPB.	49
TNF-RELATEDS	0
APOPTOSIS-INDUCING.DWPI,EPAB,JPAB,USPT,PGPB.	220
APOPTOSIS-INDUCINGS	0
LIGAND.DWPI,EPAB,JPAB,USPT,PGPB.	53049
LIGANDS.DWPI,EPAB,JPAB,USPT,PGPB.	35310
RECEPTOR.DWPI,EPAB,JPAB,USPT,PGPB.	84644
RECEPTORS.DWPI,EPAB,JPAB,USPT,PGPB.	44971
TRAIL-R.DWPI,EPAB,JPAB,USPT,PGPB.	6
TRAIL-RS	0
((TNF-RELATED ADJ APOPTOSIS-INDUCING ADJ LIGAND ADJ RECEPTOR) OR TRAIL-R).USPT,PGPB,JPAB,EPAB,DWPI.	7

Database: US Patents Full-Text Database
US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Refine Search: `TNF-related apoptosis-inducing ligand receptor or TRAIL-r` Clear

Search History

Today's Date: 7/1/2001

Term	Documents
TNF-RELATED.DWPI,EPAB,JPAB,USPT,PGPB.	49
TNF-RELATEDS	0
APOPTOSIS-INDUCING.DWPI,EPAB,JPAB,USPT,PGPB.	220
APOPTOSIS-INDUCINGS	0
LIGAND.DWPI,EPAB,JPAB,USPT,PGPB.	53049
LIGANDS.DWPI,EPAB,JPAB,USPT,PGPB.	35310
RECEPTOR.DWPI,EPAB,JPAB,USPT,PGPB.	84644
RECEPTORS.DWPI,EPAB,JPAB,USPT,PGPB.	44971
TRAIL-R.DWPI,EPAB,JPAB,USPT,PGPB.	6
TRAIL-RS	0
(TNF-RELATED APOPTOSIS-INDUCING LIGAND RECEPTOR OR TRAIL-R).USPT,PGPB,JPAB,EPAB,DWPI.	7

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DB Name	Query	Hit Count	Set Name
USPT,PGPB,JPAB,EPAB,DWPI	TNF-related apoptosis-inducing ligand receptor or TRAIL-r	7	L1

********** STN Columbus **********

FILE 'MEDLINE'
FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> s TNF-related apoptosis-inducing ligand receptor# or TRAIL-r

5 FILES SEARCHED...
L1 83 TNF-RELATED APOPTOSIS-INDUCING LIGAND RECEPTOR# OR TRAIL-R

=> dup rem l1

PROCESSING COMPLETED FOR L1
L2 41 DUP REM L1 (42 DUPLICATES REMOVED)

=> d l2 ibib ans 1-41

'ANS' IS NOT A VALID FORMAT
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=> d l2 ibib abs 1-41

L2 ANSWER 1 OF 41 MEDLINE
DUPLICATE 1
ACCESSION NUMBER: 2001292864 MEDLINE
DOCUMENT NUMBER: 21238332 PubMed ID: 11278665
TITLE: MAPK/ERK overrides the apoptotic signaling from Fas, TNF,
and TRAIL receptors.
AUTHOR: Tran S E; Holmstrom T H; Ahonen M; Kahari V M; Eriksson J E
CORPORATE SOURCE: Turku Centre for Biotechnology, POB 123, FIN-20521,
University of Turku, Turku, Finland.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 May 11) 276 (19)
16484-90.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered PubMed: 20010507
Entered Medline: 20010614
AB The tumor necrosis factor (TNF), Fas, and TNF-related apoptosis-inducing
ligand (TRAIL) receptors (R) are highly specific physiological mediators
of apoptotic signaling. We observed earlier that a number of
FasR-insensitive cell lines could redirect the proapoptotic signal to an
anti-apoptotic ERK1/2 signal resulting in inhibition of caspase
activation. Here we determine that similar mechanisms are operational in
regulating the apoptotic signaling of other death receptors. Activation of
the FasR, TNF-R1, and ***TRAIL*** - ***R*** , respectively, rapidly
induced subsequent ERK1/2 activation, an event independent from caspase
activity. Whereas inhibition of the death receptor-mediated ERK1/2
activation was sufficient to sensitize the cells to apoptotic signaling
from FasR and ***TRAIL*** - ***R*** , cells were still protected from
apoptotic TNF-R1 signaling. The latter seemed to be due to the strong
activation of the anti-apoptotic factor NF-kappaB, which remained inactive
in FasR or ***TRAIL*** - ***R*** signaling. However, when the cells
were sensitized with cycloheximide, which is sufficient to sensitize the
cells also to apoptosis by TNF-R1 stimulation, we noticed that
adenovirus-mediated expression of constitutively active MKK1 could rescue
the cells from apoptosis induced by the respective receptors by preventing
caspase-8 activation. Taken together, our results show that ERK1/2 has a
dominant protecting effect over apoptotic signaling from the death
receptors. This protection, which is independent of newly synthesized
proteins, acts in all cases by suppressing activation of the caspase
effector machinery.

L2 ANSWER 2 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2001:316522 SCISEARCH
THE GENUINE ARTICLE: 420QT
TITLE: Relative resistance of fresh isolates of melanoma to tumor
necrosis factor-related apoptosis-inducing ligand (TRAIL)-induced apoptosis
AUTHOR: Nguyen T; Zhang X D; Hersey P (Reprint)
CORPORATE SOURCE: Immunol & Oncol Unit, Room 443, David Maddison Clin Sci
Bldg, Corner King, Newcastle, NSW 2300, Australia
(Reprint); Newcastle Mater Hosp, Immunol & Oncol Unit,
Newcastle, NSW 2300, Australia
COUNTRY OF AUTHOR: Australia
SOURCE: CLINICAL CANCER RESEARCH, (MAR 2001) Vol. 7, No. 3, Supp.
[S], pp. 966S-973S.
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806,
BIRMINGHAM, AL 35202 USA.
ISSN: 1078-0432.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 27
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In previous studies, we have shown that tumor necrosis factor-related
apoptosis-inducing ligand (TRAIL) could induce varying degrees of
apoptosis in approximately two-thirds of human melanoma lines. In the
present study, we have examined the sensitivity of fresh isolates and
early passages of melanoma cells to TRAIL-induced apoptosis from eight
patients. We found that fresh isolates were relatively resistant to
TRAIL-induced apoptosis and that this appeared to be associated with low
TRAIL death receptor (***TRAIL*** - ***R***) expression.
TRAIL - ***R*** expression was also undetectable in tissue
sections from the same melanoma, We attempted to create a model for these
findings by generation of TRAIL-resistant melanoma lines from
TRAIL-sensitive lines grown for prolonged periods in TRAIL, The resulting
TRAIL-resistant melanoma cell lines had low ***TRAIL*** - ***R***
expression, and sensitivity to TRAIL was increased-rapidly by pretreatment
with proteasome inhibitors known to inhibit activation of nuclear
factor-kappaB. However, the latter treatment had no significant effect on
the sensitivity of fresh isolates to TRAIL. The levels of the inhibitors
of apoptosis, Flice-like inhibitory protein and Bcl-2, also did not relate
to resistance to TRAIL-induced apoptosis, These results suggest that
down-regulation of ***TRAIL*** - ***R*** on melanoma cells may be
the primary determinant of resistance of fresh isolates to TRAIL, and the
basis for this requires further investigation.

L2 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:311743 CAPLUS
TITLE: Relative resistance of fresh isolates of melanoma to
tumor necrosis factor-related apoptosis-inducing
ligand (TRAIL)-induced apoptosis
AUTHOR(S): Nguyen, Tam; Zhang, Xu Dong; Hersey, Peter
CORPORATE SOURCE: Oncology and Immunology Unit, Newcastle Mater
Hospital, Newcastle, 2300, Australia
SOURCE: Clin. Cancer Res. (2001), 7(3, Suppl.), 966S-973S
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In previous studies, we have shown that tumor necrosis factor-related
apoptosis-inducing ligand (TRAIL) could induce varying degrees of
apoptosis in approx. two-thirds of human melanoma lines. In the present
study, we have examd. the sensitivity of fresh isolates and early passages
of melanoma cells to TRAIL-induced apoptosis from eight patients. We
found that fresh isolates were relatively resistant to TRAIL-induced
apoptosis and that this appeared to be assocd. with low TRAIL death
receptor (***TRAIL*** - ***R***) expression. ***TRAIL*** -
R expression was also undetectable in tissue sections from the
same melanoma. We attempted to create a model for these findings by
generation of TRAIL-resistant melanoma lines from TRAIL-sensitive lines
grown for prolonged periods in TRAIL. The resulting TRAIL-resistant
melanoma cell lines had low ***TRAIL*** - ***R*** expression, and
sensitivity to TRAIL was increased rapidly by pretreatment with proteasome
inhibitors known to inhibit activation of nuclear factor-kappa.B.
However, the latter treatment had no significant effect on the sensitivity
of fresh isolates to TRAIL. The levels of the inhibitors of apoptosis,
Flice-like inhibitory protein and Bcl-2, also did not relate to resistance
to TRAIL-induced apoptosis. These results suggest that down-regulation of
TRAIL - ***R*** on melanoma cells may be the primary determinant
of resistance of fresh isolates to TRAIL, and the basis for this requires
further investigation.
REFERENCE COUNT: 27
REFERENCE(S): (1) Ashkenazi, A; J Clin Investig 1999, V104, P155
CAPLUS
(3) Emery, J; J Biol Chem 1998, V273, P14363 CAPLUS
(5) Griffith, T; Curr Opin Immunol 1998, V10, P559
CAPLUS
(6) Griffith, T; J Immunol 1998, V161, P2833 CAPLUS
(7) Griffith, T; J Immunol 1999, V162, P2597 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:443506 CAPLUS
TITLE: Progress in study of TRAIL and ***TRAIL*** -
R
AUTHOR(S): Fan, Qinglin; Song, Lihua
CORPORATE SOURCE: The Biological Institute of Anhui Province, Hefei,
230031, Peop. Rep. China
SOURCE: Zhongguo Shenghua Yaowu Zazhi (2001), 22(2), 103-105
CODEN: ZSYZFP; ISSN: 1005-1678
PUBLISHER: Zhongguo Shenghua Yaowu Zazhi Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review with 16 refs. on progress in study of TRAIL and ***TRAIL*** -
R with subdivision headings: (1) the discovery of TNF related
apoptosis-inducing ligand (TRAIL) and its receptor (***TRAIL*** -
R); (2) the mol. mechanism of TRAIL action and (3) the forecast of
its application.

L2 ANSWER 5 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:287244 BIOSIS
DOCUMENT NUMBER: PREV20010287244
TITLE: Death receptors in microvascular endothelial cells.
AUTHOR(S): Esser, P. J. (1); Luther, T. T. (1); Schraermeyer, U. (1);
Kociok, N. (1); Esser, J. M. (1); Krott, R. (1); Brunner,
R. (1); Kirchhof, B. (1); Joussen, A. M. (1)
CORPORATE SOURCE: (1) Dept. of Ophthalmology, University Eye Clinic Cologne,

Cologne Germany
SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S89. print.
Meeting Info.: Annual Meeting of the Association for
Research in Vision and Ophthalmology Fort Lauderdale,
Florida, USA April 29-May 04, 2001
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 6 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:70865 BIOSIS
DOCUMENT NUMBER: PREV200100070865
TITLE: Receptor that binds trail.
AUTHOR(S): Rauch, Charles; Walczak, Henning (1)
CORPORATE SOURCE: (1) Seattle, WA USA
ASSIGNEE: Immunex Corporation
PATENT INFORMATION: US 6072047 June 06, 2000
SOURCE: Official Gazette of the United States Patent and Trademark
Office Patents, (June 6, 2000) Vol. 1235, No. 1, pp. No
Pagination. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB A protein designated TRAIL receptor binds the protein known as TNF-Related
Apoptosis-Inducing Ligand (TRAIL). The TRAIL receptor finds use in
purifying TRAIL or inhibiting activities thereof. Isolated DNA sequences
encoding ***TRAIL*** - ***R*** polypeptides are provided, along with
expression vectors containing the DNA sequences, and host cells
transformed with such recombinant expression vectors. Antibodies that are
immunoreactive with ***TRAIL*** - ***R*** are also provided.

L2 ANSWER 7 OF 41 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-558253 [51] WPIDS
CROSS REFERENCE: 2000-256827 [22]
DOC. NO. CPI: C2000-166232
TITLE: Killing of tumor cells, e.g. solid tumors or carcinoma,
comprises administration of synergistic combination of
diterpenoid diepoxide and tumor necrosis factor related
apoptosis-inducing ligand.
DERWENT CLASS: B02
INVENTOR(S): ROSEN, G D
PATENT ASSIGNEE(S): (STRD) UNIV LELAND STANFORD JUNIOR
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000048619	A1	20000824	(200051)*	EN	29

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP SG
AU 2000033658 A 20000904 (200103)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000048619	A1	WO 2000-US3891	20000215
AU 2000033658	A	AU 2000-33658	20000215

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000033658	A Based on	WO 200048619

PRIORITY APPLN. INFO: US 1999-120313 19990216
AN 2000-558253 [51] WPIDS
CR 2000-256827 [22]
AB WO 200048619 A UPAB: 20001016
NOVELTY - Method for enhanced killing of tumor cells comprises contacting
a susceptible tumor cell with a synergistic mixture of a TRAIL (tumor
necrosis factor (***TNF***) ***related*** ***apoptosis*** -
inducing ***ligand***) ***receptor*** ligand and a
diterpenoid triepoxide (I) in a combined dosage to kill at least 50 % of
the cells.
DETAILED DESCRIPTION - Method for enhanced killing of tumor cells
comprises contacting a susceptible tumor cell with a synergistic mixture
of a TRAIL (tumor necrosis factor (***TNF***) ***related***
apoptosis - ***inducing*** ***ligand***) ***receptor***
ligand and a diterpenoid triepoxide of formula (I) in a combined dosage to
kill at least 50 % of the cells.
X1 = OH, =O or OR1;
X2, X3 = OH, OR1 or H;
R1 = C(O)-Y'-Z';
Y' = 1-6C alkyl or alkenyl (sic);
Z' = COOR2, NR3R3' or N+R4R4'R4";
R2 = a cation;
R3, R3' = H or 1-6C alkyl, hydroxyalkyl or alkoxyalkyl; or
R3+R3' = 5-7 membered heterocycle containing 2-6C, 1 or more N and
optionally 1 or more O or S (optionally substituted by 1 or more R5, OR5,
NR5R6, SR5, NO2, CN, COR5, CONR5R6, F, Cl, Br or I);
R5, R6 = H, lower alkyl, or lower alkenyl;
R4, R4', R4" = 1-6C alkyl, hydroxyalkyl or alkoxyalkyl
ACTIVITY - Cytostatic. A combination of TRAIL (100 ng/ml) and
triptolide (20 ng/ml) induced apoptosis in greater than 95 % of cells from
solid tumor cell lines (e.g. lung, breast and sarcoma cell lines) while
the individual components introduced apoptosis in less than 50 % of the
cells.
MECHANISM OF ACTION - TRAIL (tumor necrosis factor (***TNF***)
related ***apoptosis*** - ***inducing*** ***ligand***)
receptor ligand.
USE - Killing tumor cells, especially a solid tumor or a carcinoma
(especially mammary carcinoma or non-small cell lung carcinoma) (claimed).
ADVANTAGE - The mixture is synergistic, so is active at lower doses
and against otherwise resistant cell lines.
Dwg.0/0

L2 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:753424 CAPLUS
DOCUMENT NUMBER: 134:28070
TITLE: Resistance to TRAIL-induced apoptosis in primitive
neuroectodermal brain tumor cells correlates with a
loss of caspase-8 expression
AUTHOR(S): Grotzer, Michael A.; Eggert, Angelika; Zuzak, Tycho
J.; Janss, Anna J.; Marwaha, Sunil; Wiewrodt, Barbara
R.; Ikegaki, Naohiko; Brodeur, Garrett M.; Phillips,
Peter C.
CORPORATE SOURCE: Division of Oncology, The Children's Hospital of
Philadelphia, Pennsylvania, PA, 19104, USA
SOURCE: Oncogene (2000), 19(40), 4604-4610
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB TNF-related apoptosis-inducing ligand (TRAIL) is a potent inducer of
apoptosis in adult malignant glioma and various other human solid tumor
models but not in normal tissues. To characterize the TRAIL death pathway
in childhood primitive neuroectodermal brain tumor (PNET), 8 human PNET
cell lines were tested for TRAIL-induced apoptosis. TRAIL-sensitivity of
the PNET cell lines was correlated with mRNA expression levels of TRAIL,
its agonistic (TRAIL-R1, TRAIL-R2) and antagonistic (TRAIL-R3, TRAIL-R4)
receptors, cellular FLICE-like inhibitory protein (cFLIP), caspase-3 and
caspase-8. Three of 8 PNET cell lines tested were susceptible to
TRAIL-induced apoptosis. Sensitivity to TRAIL-induced apoptosis did not
correlate with mRNA expression of TRAIL receptors or cFLIP. However, all
TRAIL-sensitive PNET cell lines expressed caspase-8 mRNA and protein,
while none of the five TRAIL-resistant PNET cell lines expressed caspase-8
protein. Treatment with the methyltransferase inhibitor 5-aza-2'-deoxycytidine restored mRNA expression of caspase-8 and
TRAIL-sensitivity in formerly TRAIL-resistant PNET cells, suggesting that
gene methylation inhibits caspase-8 transcription in these cells. We
conclude, that loss of caspase-8 mRNA is an important mechanism of
TRAIL-resistance in PNET cells. Treatment with recombinant sol. TRAIL,
possibly in combination with methyltransferase inhibitors, represents a
promising therapeutic approach for PNET that deserves further
investigation.
REFERENCE COUNT: 40
REFERENCE(S): (1) Ashkenazi, A; J Clin Invest 1999, V104, P155
CAPLUS
(2) Bodmer, J; Nat Cell Biol 2000, V2, P241 CAPLUS
(3) Degli-Esposti, M; J Exp Med 1997, V186, P1165
CAPLUS
(4) Eggert, A; Biotechniques 2000, V28, P681 CAPLUS
(5) Estrov, Z; Blood 1998, V92, P3090 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:702917 CAPLUS
DOCUMENT NUMBER: 133:361874
TITLE: Maturation of dendritic cells leads to up-regulation
of cellular FLICE-inhibitory protein and concomitant
down-regulation of death ligand-mediated apoptosis
AUTHOR(S): Leverkus, Martin; Walczak, Henning; McLellan, Alex;
Fries, Hans-Werner; Terbeck, Gabi; Brocker, Eva-B.;
Kampgen, Eckhart
CORPORATE SOURCE: Department of Dermatology, University of Wurzburg
Medical School, Wurzburg, 97080, Germany
SOURCE: Blood (2000), 96(7), 2628-2631
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dendritic cells (DCs) disappear from lymph nodes 1 to 2 days after antigen
presentation, presumably by apoptosis. To evaluate the role of death
ligands in elimination of DCs, we analyzed the sensitivity of human DCs to
CD95 ligand (CD95L) and tumor necrosis factor-related apoptosis-inducing
ligand (TRAIL). We found mature DCs to be resistant to killing via CD95L
or TRAIL, whereas only immature DCs were partially sensitive. However,
all DC populations expressed CD95, TRAIL-R2, and TRAIL-R3 at comparable
levels, suggesting that sensitivity to death ligand-induced DC apoptosis
is not regulated at the receptor level. Interestingly, mature DCs highly
expressed the caspase 8 inhibitory protein cFLIP, whereas only low levels
were detected in immature DCs. Thus, death ligand sensitivity proved to
be dependent on DC maturation and inversely correlated with expression
levels of cFLIP. Induction of apoptosis by TRAIL or CD95L does not seem
to play a role in the elimination of mature DCs, but instead might serve
to regulate immature DC populations.
REFERENCE COUNT: 26
REFERENCE(S): (1) Ashkenazi, A; Curr Opin Cell Biol 1999, V11, P255
CAPLUS
(3) Bjorck, P; Int Immunol 1997, V9, P365 CAPLUS
(4) Degli-Esposti, M; Immunity 1997, V7, P813 CAPLUS
(5) Djerbi, M; J Exp Med 1999, V190, P1025 CAPLUS
(6) Griffith, T; J Exp Med 1999, V189, P1343 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:767008 SCISEARCH
THE GENUINE ARTICLE: 360ZD
TITLE: Apoptosis mediators FasL and TRAIL are upregulated in

peripheral blood mononuclear cells in MS
AUTHOR: Huang W X (Reprint); Huang P; Gomes A; Hillert J
CORPORATE SOURCE: HUDDINGE UNIV HOSP, DEPT NEUROL, KAROLINSKA INST, S-14186
HUDDINGE, SWEDEN (Reprint); KAROLINSKA INST, NOVUM, CTR
BIOTECHNOL, HUDDINGE, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: NEUROLOGY, (10 OCT 2000) Vol. 55, No. 7, pp. 928-934.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST,
PHILADELPHIA, PA 19106-3621.
ISSN: 0028-3878.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 39
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Objective: To investigate the expression of apoptosis-inducing- ligand
and receptor molecules in patients with MS. Background: Dysregulation of
apoptosis may induce autoimmune conditions, possibly through inadequate
termination of immune responses, and could be of importance for
pathogenesis of MS. Methods: Messenger RNA (mRNA) levels of two
apoptosis-related members of the tumor necrosis factor (TNF) receptor
family, Fas and TNF-related apoptosis-inducing ligand (TRAIL) receptor 2 (
TRAIL - ***R*** -2), and their ligands, Fas ligand (FasL) and
TRAIL, were quantified by competitive reverse transcription PCR in
unstimulated peripheral blood mononuclear cells in 47 untreated patients
with MS and 46 control subjects, Results: The expression of FasL was
increased in patients with MS compared with healthy control subjects.
Analysis of clinical subgroups revealed that the increase was marked in
relapsing-remitting MS, being especially high in remission ($p = 0.0002$),
but less so in chronic progressive MS ($p = 0.14$). Compared with healthy
control subjects, TRAIL mRNA levels were also upregulated in patients with
MS ($p = 0.0001$) but did not differ between clinical subgroups. The
expression of ***TRAIL*** - ***R*** , was slightly elevated in
patients with MS ($p = 0.02$) whereas the expression of Fas was similar in
patients and control subjects. The ratio of expression levels for two
isoforms of ***TRAIL*** - ***R*** „ TRICK2a and TRICK2b, in patients
with MS differed from healthy control subjects ($p = 0.04$). Conclusions:
There was increased expression of both FasL and TRAIL in peripheral blood
lymphocytes. It remains to be determined whether this increased expression
represents a disease-promoting autoimmune process or is merely the effect
of a secondary compensatory mechanism that downregulates the inflammatory
response.

L2 ANSWER 11 OF 41 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2000338587 MEDLINE
DOCUMENT NUMBER: 20338587 PubMed ID: 10881678
TITLE: Extensive lymphopenia due to apoptosis of uninfected
lymphocytes in acute measles patients.
AUTHOR: Okada H; Kobune F; Sato T A; Kohama T; Takeuchi Y; Abe T;
Takayama N; Tsuchiya T; Tashiro M
CORPORATE SOURCE: Department of Viral Diseases and Vaccine Control, National
Institute of Infectious Diseases, Tokyo, Japan.
SOURCE: ARCHIVES OF VIROLOGY, (2000) 145 (5) 905-20.
Journal code: 8L7; 7506870. ISSN: 0304-8608.
PUB. COUNTRY: Austria
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000720
AB Infection with measles virus induces a transient immunosuppression, which
occasionally results in fatal opportunistic infections. To obtain
fundamental information about the mechanism, we examined peripheral blood
mononuclear cells (PBMC) from acute measles patients aged from infants to
35 years old, obtained at various times from incubation periods to 103
days after onset of rash, for the number of lymphocyte subsets by
flowcytometry. The data were analyzed for relationships between aging of
the patients and the severity of immunosuppression. In classical measles
cases, infected lymphocytes detected as a minor population during the
incubation period disappeared soon after onset of rash, whereas in the
cases of serious illness, the infected cells persisted longer after the
rash. At the onset of rash, remarkable lymphopenia had already occurred in
all measles cases with reduction in cell numbers of CD4+ T cells, CD8+ T
cells, B cells, neutrophils, and monocytes. In contrast, natural killer
(NK) cells were increased in number and activated, which might be a
response compensatory for the lymphopenia. Apoptosis-associated molecules
such as CD95(Fas) and ***TNF*** - ***related*** ***apoptosis*** -
inducing ***ligand*** - ***receptor*** (***TRAIL*** -
R) were highly expressed on the cell surface of most surviving
non-infected lymphocytes, and DNA fragmentation was also observed upon
incubation in vitro. These results suggested that the profound lymphopenia
was primarily due to extended death of non-infected blood cells caused by
apoptosis. The severity and duration of the lumphopenia were
age-dependent; less severe in young children whereas much severer in
infants under one year of age as well as adolescents and adults. From
these results, it was suggested that remarkable lymphopenia due to
apoptosis of uninfected cells is one of the principal causes for
immunosuppression induced by measles virus infection, and is correlated
with the age-dependent severity of the disease.

L2 ANSWER 12 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:949420 SCISEARCH
THE GENUINE ARTICLE: 357JU
TITLE: Expression of TRAIL/ ***TRAIL*** - ***R*** in
inflammatory myopathies.
AUTHOR: Murakawa Y (Reprint); Kondo M; Kayagaki N; Kawakami M;
Okumura K; Kobayashi S
SOURCE: ARTHRITIS AND RHEUMATISM, (SEP 2000) Vol. 43, No. 9, Supp.
[S], pp. 775-775.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST,
PHILADELPHIA, PA 19106-3621.
ISSN: 0004-3591.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L2 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:583433 CAPLUS
DOCUMENT NUMBER: 134:146230
TITLE: Expression of TRAIL receptors in human autoreactive
and foreign antigen-specific T cells
AUTHOR(S): Wendling, U.; Walczak, H.; Dorr, J.; Jaboci, C.;
Weller, M.; Krammer, P. H.; Zipp, F.
CORPORATE SOURCE: Division of Neuroimmunology, Department of Neurology,
Charite, Berlin, Germany
SOURCE: Cell Death Differ. (2000), 7(7), 637-644
CODEN: CDDIEK; ISSN: 1350-9047
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Deletion of T cells due to apoptosis induction is a regulatory mechanism
in the human immune system that may be impaired in autoimmune diseases such as multiple sclerosis (MS). Involvement of the apoptosis-mediating
CD95/CD95 ligand system in MS has been demonstrated. Here, the authors
report that (auto)antigen-specific human T cells are not killed in vitro
by sol. TNF-related apoptosis-inducing ligand (TRAIL) although expressing
death-inducing receptors, TRAIL receptor 1 (TRAIL-R1) and TRAIL-R2.
Apoptosis was assessed by caspase activation and DNA fragmentation,
receptor expression was detected by RT-PCR and flow cytometry. The
(auto)antigen-specific T cells were also resistant to specific
TRAIL-R1/TRAIL-R2-directed induction of apoptosis, indicating that
coexpression of the truncated TRAIL-R3 and TRAIL-R4 in these T cells is
not responsible for the obsd. resistance. Upon stimulation, levels of
death-inducing TRAIL receptors decreased whereas TRAIL was up-regulated on
the cell surface. In contrast to CD95, the role of TRAIL receptors in MS
might not involve regulation of T cell vulnerability.
REFERENCE COUNT: 51
REFERENCE(S): (1) Alderson, M; J Exp Med 1995, V181, P71 CAPLUS
(2) Ciusani, E; J Neuroimmunol 1998, V82, P5 CAPLUS
(3) Critchfield, J; Science 1994, V263, P1139 CAPLUS
(4) Degli-Esposti, M; Immunity 1997, V7, P813 CAPLUS
(5) Degli-Esposti, M; J Exp Med 1997, V186, P1165
CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:238935 BIOSIS
DOCUMENT NUMBER: PREV200000238935
TITLE: Expression and function of the TRAIL ligand/receptor system
in neuroblastoma.
AUTHOR(S): Eggert, Angelika (1); Zuzak, T. (1); Grotzer, M. A. (1);
Ikegaki, N. (1); Brodeur, G. M. (1)
CORPORATE SOURCE: (1) Children's Hosp of Philadelphia, Philadelphia, PA USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (March, 2000) No. 41, pp. 557.
Meeting Info.: 91st Annual Meeting of the American
Association for Cancer Research. San Francisco, California,
USA April 01-05, 2000
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 15 OF 41 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 2000139806 MEDLINE
DOCUMENT NUMBER: 20139806 PubMed ID: 10676636
TITLE: Regulation of tumor necrosis factor-related apoptosis-inducing ligand sensitivity in primary and
transformed human keratinocytes.
AUTHOR: Leverkus M; Neumann M; Mengling T; Rauch C T; Brocker E B;
Krammer P H; Walczak H
CORPORATE SOURCE: Department of Dermatology, University of Wurzburg Medical
School, Germany.
SOURCE: CANCER RESEARCH, (2000 Feb 1) 60 (3) 553-9.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000810
Entered Medline: 20000228
AB Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) has been
shown to exert potent cytotoxic activity against many tumor cell lines but
not against normal cells. It has been hypothesized that this difference in
TRAIL sensitivity between normal and transformed cells might be due to the
expression of the non-death-inducing TRAIL receptors (***TRAIL*** -

R) TRAIL-R3 and TRAIL-R4, presumably by competition for limited amounts of TRAIL. To assess the regulation of resistance versus sensitivity to TRAIL in primary as well as transformed keratinocytes, we examined TRAIL sensitivity, TRAIL receptor expression, and intracellular signaling events induced by TRAIL. Although TRAIL induced apoptosis in primary as well as transformed keratinocytes, a marked difference in sensitivity could be observed with primary keratinocytes (PK) being 5-fold less sensitive to TRAIL than transformed keratinocytes (TK). Yet both cell types exhibited similar TRAIL receptor surface expression, suggesting that expression of TRAIL-R3 and TRAIL-R4 may not be the main regulator of sensitivity to TRAIL. Biochemical analysis of the signaling events induced by TRAIL revealed that PK could be sensitized for TRAIL and, similarly, for TRAIL-R1- and TRAIL-R2-specific apoptosis by pretreatment of the cells with cycloheximide (CHX). This sensitization concomitantly resulted in processing of caspase-8, which did not occur in TRAIL-resistant PK. These data indicate that an early block of TRAIL-induced apoptosis was present in PK compared with TK or PK treated with CHX. Interestingly, cellular FLICE inhibitory protein (cFLIP) levels, high in PK and low in TK and several other squamous cell carcinoma cell lines, decreased rapidly after treatment of PK with CHX, correlating with the increase in TRAIL sensitivity and caspase-8 processing. Furthermore, ectopic expression of cFLIP long (cFLIP(L)) in TK by transfection with a cFLIP(L) expression vector resulted in resistance to TRAIL-mediated apoptosis of these cells. Thus, our results demonstrate that TRAIL sensitivity in PK is primarily regulated at the intracellular level rather than at the receptor level.

L2 ANSWER 16 OF 41 MEDLINE
DUPLICATE 4
ACCESSION NUMBER: 2000427861 MEDLINE
DOCUMENT NUMBER: 20417933 PubMed ID: 10960439
TITLE: Chemotherapeutic agents augment TRAIL-induced apoptosis in human hepatocellular carcinoma cell lines.
AUTHOR: Yamanaka T; Shiraki K; Sugimoto K; Ito T; Fujikawa K; Ito M; Takase K; Moriyama M; Nakano T; Suzuki A
CORPORATE SOURCE: First Department of Internal Medicine, Mie University School of Medicine, Tsu, Japan.
SOURCE: HEPATOLOGY, (2000 Sep) 32 (3) 482-90. Journal code: GBZ; 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000914
AB TNF-related apoptosis-inducing ligand (TRAIL) selectively induces apoptosis in various transformed cell lines but not in almost-normal tissues. It is regulated by 2 death receptors, TRAIL receptor 1 (TRAIL-R1) and TRAIL-R2, and 2 decoy receptors, TRAIL-R3 and TRAIL-R4. We investigated the expression of ***TRAIL*** - ***R*** - and TRAIL-induced apoptosis in human hepatocellular carcinomas (HCCs). TRAIL-R1, -R2, and -R4 were expressed in 6 HCC cell lines examined, but TRAIL-R3 was expressed in only 2 of the 6 cell lines. In addition, immunohistochemical results revealed a high and prevalent expression of TRAIL-R1 and -R2 in human HCC tissues. Despite the expression of TRAIL-R1 and -R2, all 6 HCC cell lines showed resistance to TRAIL-induced apoptosis with no relation to nuclear factor kappa B (NF-kappaB) levels induced by TRAIL. TRAIL-induced death signal was inhibited with both decreased caspase-8 and caspase-3 activity. However, TRAIL induced significant apoptosis in the presence of a subtoxic level of actinomycin D, indicating that the TRAIL-induced apoptotic pathway is in place in these cell lines. In addition, we found that treatment with conventional chemotherapeutic agents, doxorubicin and camptothecin, dramatically augmented TRAIL-induced cytotoxicity in most of the HCC cell lines. Actinomycin D and camptothecin almost completely suppressed NF-kappaB induction by TRAIL, whereas doxorubicin had little effect. These results indicate that TRAIL, in combination with chemotherapeutic agents, may have therapeutic potential in the treatment of human HCC.

L2 ANSWER 17 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
DUPLICATE 5
ACCESSION NUMBER: 2001:127375 BIOSIS
DOCUMENT NUMBER: PREV200100127375
TITLE: Expression of different receptors of the apoptosis inducing gene TRAIL in human ovarian tumors.
AUTHOR(S): Li Xin-guo (1); Zhang Yu (1); Chen Bing-lai (1)
CORPORATE SOURCE: (1) Department of Gynecology and Obstetrics, Xiangya Hospital, Hunan Medical University, Changsha, 410008 China
SOURCE: Hunan Yike Daxue Xuebao, (Oct. 28, 2000) Vol. 25, No. 5, pp. 471-473. print.
ISSN: 1000-5625.
DOCUMENT TYPE: Article
LANGUAGE: Chinese
SUMMARY LANGUAGE: Chinese; English
AB Reverse transcriptase polymerase chain reaction (RT-PCR) was applied to assay mRNA expression of TRAIL (the ***TNF*** ***related*** ***apoptosis*** ***inducing*** ***ligand***) ***receptors*** (DR5, DcR1, and DcR2) in 3 cases of normal ovarian tissues, 6 cases of ovarian benign tumors, and 16 cases of ovarian cancers. Peripheral blood lymphocytes were used as a positive control. Positive expression of the DR5 and DcR1 were found in peripheral blood lymphocytes and 3 cases of normal ovaries. Positive expressions of the DR5 and DcR1 were 83.3% (5/6) in benign ovarian tumors and 68.8% (11/16) in ovarian cancers respectively. Positive expression of the DcR2 was only found in normal ovaries and benign tumors. These findings suggest that expression of different receptors may play an important role in the apoptosis regulation of ovarian tumors, especially DcR2.

L2 ANSWER 18 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 6
ACCESSION NUMBER: 2000:894211 SCISEARCH
THE GENUINE ARTICLE: 375MJ
TITLE: Expression ol TRAIL (***TNF*** - ***related*** ***apoptosis*** - ***inducing*** ***Ligand***) ***receptors*** in cervical cancer
AUTHOR: Ryu H S; Chang K H (Reprint); Chang S J; Kim M S; Joo H J; Oh K S
CORPORATE SOURCE: AJOU UNIV, SCH MED, DEPT OBSTET & GYNECOL, SAN 5, SUWON 442721, SOUTH KOREA (Reprint); AJOU UNIV, SCH MED, DEPT OBSTET & GYNECOL, SUWON 442721, SOUTH KOREA; AJOU UNIV, SCH MED, DEPT PATHOL, SUWON 442721, SOUTH KOREA
COUNTRY OF AUTHOR: SOUTH KOREA
SOURCE: INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER, (SEP-OCT 2000) Vol. 10, No. 5, pp. 417-424. Publisher: BLACKWELL SCIENCE INC, 350 MAIN ST, MALDEN, MA 02148.
ISSN: 1048-891X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Apoptosis is an intrinsic and fundamental biologic process that plays a critical role in the normal development of multicellular organisms and in the maintainance of tissue homeostasis. Some of the well known regulators of apoptosis are cytokines of the tumor necrosis factor (TNF) ligand family, such as Fas ligand (Fas L) and TNF, which induce apoptosis by activation of their corresponding receptors, Fas and TNFR-1. Recently, a new member of the TNF family known as TRAIL (TNF-related apoptosis-inducing ligand) was identified and shown to induce p53-independent apoptosis in a variety of tumor cell lines but not in normal cells. Four human receptors for TRAIL were also recently identified and designated TRAIL-R1, -R2, -R3, and -R4. The aim of this study is to examine whether TRAIL and TRAIL receptors (-R1, -R2, -R3) are expressed in uterine cervical cancer and whether it is correlated with apoptosis, TRAIL, and TRAIL receptors. The subjects were 20 patients who were diagnosed with cervical cancer. Western blotting was performed in nine cases and immunohistochemical staining for TRAIL and TRAIL, receptors (-R1, -R2, -R3) and TUNEL method for detection of apoptosis was performed in 11 cases. There were proteins for TRAIL, TRAIL-R1, -R2, and -R3 in tissues from cervical cancer. All TRAIL receptors were expressed in both normal cervical epithelium and tumor cells, and TRAIL-R1 and -R2 were more strongly expressed in tumor cells than normal epithelium ($P < 0.05$). Apoptosis correlated with expression of TRAIL-R1 and -R2 ($P < 0.05$). This study suggests that TRAIL induces apoptosis in cervical cancer through its receptors.

L2 ANSWER 19 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:252329 BIOSIS
DOCUMENT NUMBER: PREV200000252329
TITLE: Inhibition of NF-kappaB activity enhances trail induced apoptosis in breast cancer cell lines.
AUTHOR(S): Keane, Maccon M. (1); Rubinstein, Yaffa R. (1); Ettenberg, Seth A. (1); Nau, Marion M. (1); Lipkowtiz, Stan (1)
CORPORATE SOURCE: (1) National Cancer Inst, Bethesda, MD USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 244. Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 20 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:790597 SCISEARCH
THE GENUINE ARTICLE: 363RA
TITLE: Mechanisms of resistance of normal cells to TRAIL induced apoptosis vary between different cell types
AUTHOR: Zhang X D; Nguyen T; Thomas W D; Sanders J E; Hersey P (Reprint)
CORPORATE SOURCE: NEWCASTLE MATER HOSP, IMMUNOL & ONCOL UNIT, DAVID MADDISON BLDG, ROOM 443, CNR KING & WATT ST, NEWCASTLE, NSW 2300, AUSTRALIA (Reprint); NEWCASTLE MATER HOSP, IMMUNOL & ONCOL UNIT, NEWCASTLE, NSW 2300, AUSTRALIA
COUNTRY OF AUTHOR: AUSTRALIA
SOURCE: FEBS LETTERS, (6 OCT 2000) Vol. 482, No. 3, pp. 193-199. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0014-5793.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English

REFERENCE COUNT: 33
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Resistance of normal cells to tumour necrosis factor related apoptosis inducing ligand (TRAIL) induced apoptosis is believed to be mediated by expression of two decoy receptors. Here we show that the expression and localisation of TRAIL receptors (TRAIL-Rs) vary between different cells and that resistance to TRAIL is mediated by different mechanisms. The decoy receptor, TRAIL-R3, appeared important in protection of endothelial cells, whereas lack of surface death receptor expression and as yet unknown intracellular inhibitor(s) of apoptosis downstream of caspase-3 may play a major role in protection of melanocytes and fibroblasts from TRAIL induced apoptosis, respectively. Differential subcellular location of decoy receptors may be an important determinant of their effectiveness in different types of normal cells. (C) 2000 Federation of European Biochemical Societies. Published by Elsevier Science B.V. All rights reserved.

L2 ANSWER 21 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:300248 BIOSIS
DOCUMENT NUMBER: PREV200100300248
TITLE: Variations in trail-induced apoptosis of freshly obtained myeloma cells are not related to trail receptor expression or prior chemotherapy.
AUTHOR(S): Lincz, Lisa F. (1); Yeh, Te-Hsien; Enno, Arno (1); Spencer, Andrew
CORPORATE SOURCE: (1) Hunter Haematology Research Group, Mater Misericordiae Hospital, Newcastle, NSW Australia
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 162a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB TNF-related apoptosis-inducing ligand (TRAIL) is a potent and selective inducer of apoptosis in malignant cells. Using the combined methods of Annexin V labelling, cell cycle analysis and DNA electrophoresis, we have demonstrated susceptibility to TRAIL-induced apoptosis in the human multiple myeloma (MM) cell lines NCI H929, RPMI 8226, OPM-2 and LP-1, while the lymphoblastoid cell lines (LCL) U266 and MC/CAR were resistant. Two different forms of TRAIL were tested: purified human recombinant soluble TRAIL (s-TRAIL; residues 114-281; Biomol, Plymouth Meeting, PA) demonstrated maximal apoptosis induction at 1 mug/ml in sensitive cell lines, while a leucine zipper construct (LZ-TRAIL; Immunex Corp., Seattle, WA) was equally effective when used at a concentration of 500 ng/ml. BM samples obtained from 16 MM patients at various stages of disease were incubated for 24 hours with or without either 2mug/ml s-TRAIL (n=8) or 1mug/ml LZ-TRAIL (n=8). The percentage of viable MM cells was then determined by flow cytometric quantification of anti-CD138 stained cells and relative TRAIL-induced reduction in MM cells calculated using the formula: ((Untreated)-(TRAIL-Treated))/Untreated X 100%. BM samples from 6 of 16 (38%) patients demonstrated a significant (>10%) relative reduction in the number of MM cells following TRAIL incubation (range: 11% to 59%). This did not correlate with prior therapy, as a reduction was seen in 2/5 samples obtained from patients at diagnosis, 2/5 samples following standard-dose chemotherapy and 2/6 samples following high-dose chemotherapy. The relationship between TRAIL-receptor expression (TRAIL-R1, R2, R3, R4 and OPG) and TRAIL-induced apoptosis was examined in 2 sensitive (NCI H929, RPMI 8226) and the 2 resistant cell lines and 5 MM BM samples (2 sensitive, 3 resistant) utilising RT-PCR and surface immunostaining of purified MM cells. Concordance between TRAIL-receptor mRNA detection and cell surface expression was shown in all cell lines. Furthermore, all cell lines and patient samples demonstrated mRNA expression for the intracellular death-domain containing TRAIL-R1. Variable expression of the 2 decoy (TRAIL-R3 and R4) and soluble (OPG) receptors was seen and this did not correlate with TRAIL sensitivity. We conclude that MM cell expression of death effector receptors for TRAIL is insufficient to confer sensitivity to TRAIL-induced apoptosis but that in a significant minority of patients, irrespective of prior therapy, MM cells are sensitive to TRAIL-induced apoptosis.

L2 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:249346 CAPLUS
DOCUMENT NUMBER: 133:220794
TITLE: Expression of Trail receptor on human T cells and apoptosis induced by trail
AUTHOR(S): Fan, Xuegong
CORPORATE SOURCE: Department of Infectious Diseases, Xiangya Hospital, Hunan Medical University, Changsha, 410008, Peop. Rep. China
SOURCE: Zhongguo Mianyixue Zazhi (2000), 16(3), 122-124
CODEN: ZMZAEE; ISSN: 1000-484X
PUBLISHER: Zhongguo Mianyixue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The expression of Trail (***TNF*** - ***related*** ***apoptosis*** - ***inducing*** ***ligand***) ***receptor*** on human T cells and apoptosis induced by Trail were studied. The pos. cells for Trail receptor and apoptotic cells were detd. by flow cytometry. Trail receptor on unstimulated Jurkat cells was found in % and the stimulation could not increase the expression of Trail receptor on Jurkat cells. The apparent apoptosis of Jurkat cells was found in (90.01 .+-. 26.71)%. Peripheral blood lymphocytes (PBL) from healthy donors may express Trail receptor after activation (25.27 .+-. 6.42)%, but no apoptosis was obsd. in these PBL. Human T cells may express Trail receptor. The ligation of Trail receptor and Trail plays an important role in regulation of apoptosis.

L2 ANSWER 23 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:382776 BIOSIS
DOCUMENT NUMBER: PREV200000382776
TITLE: Coordinated regulation of two TRAIL-R2/KILLER/DR5 mRNA isoforms by DNA damaging agents, serum and 17beta-estradiol in human breast cancer cells.
AUTHOR(S): Wang, Thomas T. Y. (1); Jeng, Jiingjau
CORPORATE SOURCE: (1) Phytonutrients Laboratory, Beltsville Human Nutrition Research Center, ARS, USDA, Building 307, Room 326, Beltsville, MD, 20705 USA
SOURCE: Breast Cancer Research and Treatment, (May, 2000) Vol. 61, No. 1, pp. 87-96. print.
ISSN: 0167-6806.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A search of the Genebank database revealed that there are two distinct gene sequences with the common name of TRAIL-R2/Killer/DR5. Using reverse transcription-polymerase chain reaction (RT-PCR), we confirmed the existence of two isoforms of TRAIL-R2/Killer/DR5 mRNA, which we have designated the long and short isoforms based on their electrophoretic mobility. We found that both the long and short mRNA isoforms are ubiquitously expressed in human tissues and cell lines. The long form generally predominates, but the proportion of the two isoforms varies depending on the tissue type. Treatment of MCF-7 human breast cancer cells with the DNA damaging drugs adriamycin, campthothecin, or etoposide causes a coordinated up-regulation of both isoforms. Treatment of the p53-mutant T-47D breast cancer cell line with adriamycin also results in up-regulation of both isoforms, suggesting that adriamycin up-regulates TRAIL-R2/Killer/DR5 expression independent of functional p53. The expression of both mRNA isoforms are increased in MCF-7 cells cultured in charcoal-stripped fetal bovine serum compared to normal serum, suggesting that sex steroid hormones may play a role in the negative regulation of their expression. This was confirmed in MCF-7 cells cultured in stripped serum supplemented with 17beta-estradiol, which also resulted in a decrease in the mRNA expression of both isoforms. These results demonstrate that the TRAIL-R2/Killer/DR5 gene gives rise to two distinct forms of mRNA, and that these two forms are coordinately regulated by DNA damage and 17beta-estradiol in human breast cancer cells. The functional significance of the two isoforms remains to be determined.

L2 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:656238 CAPLUS
DOCUMENT NUMBER: 133:250528
TITLE: Fas- and ***TRAIL*** - ***R*** -induced apoptosis is blocked by Bcl-xL in pancreatic carcinoma cells
AUTHOR(S): Ungefroren, H.; Hinz, S.; Bonecke, L.; Klosa, K.; Kalthoff, H.
CORPORATE SOURCE: Forschungsgruppe Molekulare Onkologie, Klinik fur Allgemeine Chirurgie und Thoraxchirurgie, Christian-Albrechts-Universitat, Kiel, D-24105, Germany
SOURCE: Chir. Forum Exp. Klin. Forsch. (2000) 65-68
CODEN: CFEKA7; ISSN: 0303-6227
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The resistance of pancreatic adenocarcinomas to std. chemo- and radiotherapy results from perturbations in apoptosis. In this study the authors tried to identify proteins that interfere neg. with the signal transduction of the Fas (CD95, APO-1) and TRAIL receptors, resp. 3 Different pancreatic carcinoma cell lines and Colo357 cells retrovirally transduced with a Bcl-xL expression vector were treated with the agonistic anti-Fas antibody CH11 or with TRAIL in the presence or absence of cycloheximide. Subsequently, apoptosis was measured with the JAM DNA fragmentation assay. All pancreatic carcinoma cell lines investigated displayed cross-resistance against Fas- and ***TRAIL*** - ***R*** -induced apoptosis which could to various extents be alleviated by cycloheximide treatment. Overexpression of Bcl-xL in the more sensitive cell line Colo357 rendered these cells completely resistant to Fas- and ***TRAIL*** - ***R*** -induced apoptosis. High Bcl-xL expression in pancreatic carcinoma is not only responsible for resistance to std. chemo- and radiotherapy but also represents an immune escape mechanism leading to a survival advantage of tumor cells. Inhibition of the anti-apoptotic function of Bcl-xL therefore offers an interesting therapeutic option.
REFERENCE COUNT: 3
REFERENCE(S): (1) Ashkenazi, A; J Clin Invest 1999, V104, P155 CAPLUS
(2) Scaffidi, C; EMBO J 1998, V17, P1675

CAPLUS
(3) Ungefroren, H; Cancer Res 1998, V58, P1741 CAPLUS

L2 ANSWER 25 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:276014 BIOSIS
DOCUMENT NUMBER: PREV200000276014
TITLE: Resistance to trail-mediated apoptosis in human hepatocellular carcinomas.
AUTHOR(S): Yamanaka, Takenari (1); Shiraki, Katsuya (1); Inoue, Hidekazu (1); Ito, Takeshi (1); Sugimoto, Kazushi (1); Sakai, Takahisa (1); Ohmori, Shigeru (1); Wagayama, Hidetaka (1); Fujikawa, Katsuhiko (1); Takase, Koujiro (1); Nakano, Takeshi (1)
CORPORATE SOURCE: (1) First Dept of Internal Medicine, Mie Univ, Tsu Japan
SOURCE: Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 1, pp. AASLD A910. print.. Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May 21-24, 2000 American Gastroenterological Association . ISSN: 0016-5085.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L2 ANSWER 26 OF 41 WPIDS COPYRIGHT 2001
DERWENT INFORMATION LTD DUPLICATE 7
ACCESSION NUMBER: 1999-276942 [23] WPIDS
CROSS REFERENCE: 1999-229238 [19]
DOC. NO. CPI: C1999-081240
TITLE: Novel tumor necrosis factor receptor proteins TRAIL-R2 and TRAIL-R3.
DERWENT CLASS: B04 D16
INVENTOR(S): TSCHOPP, J
PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC; (APOT-N) APOTECH R & D SA
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9912963	A2	19990318	(199923)*	EN	28

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9893863 A 19990329 (199932)
EP 1012179 A2 20000628 (200035) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9912963	A2	WO 1998-US19029	19980911
AU 9893863	A	AU 1998-93863	19980911
EP 1012179	A2	EP 1998-946966	19980911
		WO 1998-US19029	19980911

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9893863	A Based on	WO 9912963
EP 1012179	A2 Based on	WO 9912963

PRIORITY APPLN. INFO: US 1998-84422 19980506; US 1997-58631 19970912
AN 1999-276942 [23] WPIDS
CR 1999-229238 [19]
AB WO 9912963 A UPAB: 20000725
NOVELTY - Novel mammalian cysteine-rich receptors of the tumour necrosis factor family TRAIL-R2 and TRAIL-R3 proteins have the 440 and 259 amino acid sequences given in the specification respectively.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for: (1) antibody preparation reactive to TRAIL-R2 or -R3 or bilogically active fragment; (2) a soluble ***TRAIL*** - ***R*** comprising a human immunoglobulin Fc domain; and (3) a method of expressing TRAIL-R2 or -R3 in a mammalian cell by introducing the TRAIL-R2 or -R3-encoding DNA into a cell and expressing the TRAIL-R2 or -R3 in the cell.
ACTIVITY - Cytostatic; anti-apoptosis; immunomodulator.
MECHANISM OF ACTION - Tumour necrosis factor receptor blocker.
USE - The TRAIL-R2 or -R3 can be used for treating or reducing the advancement, severity or effects of an immunological disease in a mammal, or for treating cancer or for inducing cell death.
Dwg.0/5

L2 ANSWER 27 OF 41 WPIDS COPYRIGHT 2001
DERWENT INFORMATION LTD DUPLICATE 8
ACCESSION NUMBER: 1999-132236 [11] WPIDS
DOC. NO. CPI: C1999-038767
TITLE: New isolated TRAIL receptor polypeptides - used to develop products for treating e.g. thrombotic microangiopathy, multiple sclerosis, systemic lupus erythematosus or HIV infection.
DERWENT CLASS: B04 D16
INVENTOR(S): DEGLI-ESPOSTI, M
PATENT ASSIGNEE(S): (IMMV) IMMUNEX CORP
COUNTRY COUNT: 28
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9903992	A1	19990128	(199911)*	EN	50

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA IL IS JP KR MX NO NZ
AU 9883957 A 19990210 (199925)
EP 998561 A1 20000510 (200027) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9903992	A1	WO 1998-US14410	19980710
AU 9883957	A	AU 1998-83957	19980710
EP 998561	A1	EP 1998-934441	19980710
		WO 1998-US14410	19980710

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9883957	A Based on	WO 9903992
EP 998561	A1 Based on	WO 9903992

PRIORITY APPLN. INFO: US 1997-892119 19970715
AN 1999-132236 [11] WPIDS
AB WO 9903992 A UPAB: 19990316
An isolated DNA (A) comprises a nucleotide sequence (NS) encoding tumour necrosis factor (TNF)-Related Apoptosis-Inducing ligand (TRAIL) receptor polypeptide (***TRAIL*** - ***R***), where the ***TRAIL*** - ***R*** is selected from: (a) a ***TRAIL*** - ***R*** polypeptide (I) having a sequence (S1) of 386 amino acids (aa); (b) a ***TRAIL*** - ***R*** polypeptide (II) having a 386 aa sequence (S2), and (c) a fragment of a polypeptide of (a) or (b), where the fragment is capable of binding TRAIL. Also claimed are: (1) an isolated DNA encoding a ***TRAIL*** - ***R*** polypeptide which comprises an aa sequence that is at least 90% identical to an aa sequence selected from: (a) aa residues 1-386, 56-386, 1-211, or 56-211 of (I); (b) aa residues 1-386, 56-386, or 1-211 of (II); (2) an isolated DNA comprising at least 60 contiguous nucleotides (nt) of a 1552 (III) or 1296 (IV) nt NS; (3) an expression vector comprising a DNA as in (A) or (1); (4) a purified ***TRAIL*** - ***R*** polypeptide selected from: (a) a ***TRAIL*** - ***R*** polypeptide of (I) in mature form; (b) a ***TRAIL*** - ***R*** polypeptide of (II) in mature form; and (c) a fragment of a polypeptides as in (a) or (b) which is capable of binding TRAIL; (5) a purified ***TRAIL*** - ***R*** polypeptide comprising an aa sequence that is at least 90% identical to aa sequence selected from: (a) aa residues 56-386 of (I) or (II), and (b) residues 56-211 of (I); (6) an oligomer comprising at least 2 ***TRAIL*** - ***R*** polypeptides as in (5), and (7) an antibody that is directed against a ***TRAIL*** - ***R*** polypeptide as in (4) or an antigen-binding fragment of the antibody.
USE - The ***TRAIL*** - ***R*** polypeptides can be used for binding TRAIL, e.g. to measure or inhibit the biological activity of TRAIL. The ***TRAIL*** - ***R*** polypeptides can be used for treating thrombotic microangiopathies, e.g. thrombotic thrombocytopenic purpura (TTP) or haemolytic-uremic syndrome (HUS), clotting of small blood vessels in e.g. AIDS, multiple sclerosis or systemic lupus erythematosus or for reducing TRAIL-mediated death of T cells in HIV-infected patients.
They can also be used to purify TRAIL or TRAIL-expressing cells or as carriers for delivering agents to cells bearing TRAIL. The products can also be used for detection and diagnosis.
Dwg.0/2

L2 ANSWER 28 OF 41 MEDLINE
DUPLICATE 9
ACCESSION NUMBER: 1999248188 MEDLINE
DOCUMENT NUMBER: 99248188 PubMed ID: 10229846
TITLE: TRAIL (Apo-2L) and TRAIL receptors in human placentas: implications for immune privilege.
AUTHOR: Phillips T A; Ni J; Pan G; Ruben S M; Wei Y F; Pace J L; Hunt J S
CORPORATE SOURCE: Departments ofAnatomy and Cell Biology, Pathology and Laboratory Medicine, and Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS 66160, USA.
CONTRACT NUMBER: HD02528 (NICHD)
HD24212 (NICHD)
HD29156 (NICHD)
SOURCE: JOURNAL OF IMMUNOLOGY, (1999 May 15) 162 (10) 6053-9.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990614
AB Mechanisms accounting for protection of the fetal semiallograft from maternal immune cells remain incompletely understood. In other contexts, interactions between TRAIL (TNF-related apoptosis-inducing ligand/Apo-2L) and its receptors kill activated lymphocytes. The purpose of this study was therefore to investigate the potential of the TRAIL/***TRAIL*** - ***R*** system to protect the placenta against immune cell attack. Analysis by Northern blotting demonstrated mRNAs encoding TRAIL as well as the four TRAIL receptors (DR4, DR5, DcR1/TRID, DcR2/TRUNDD) in human placentas. Immunohistochemical experiments demonstrated that TRAIL protein is prominent in syncytiotrophoblast, an uninterrupted placental cell layer that is continuously exposed to maternal blood, as well as in macrophage-like placental mesenchymal cells (Hofbauer cells). Studies on cell lines representing trophoblasts (Jar, JEG-3 cells) and macrophages (U937, THP-1 cells) showed that both lineages contained TRAIL mRNA and that steady state levels of transcripts were increased 2- to 11-fold by IFN-gamma. By contrast, cell lineage-specific differences were observed in

expression of the ***TRAIL*** - ***R*** genes. Although all four
lines contained mRNA encoding the apoptosis-inducing DR5 receptor, only
trophoblast cells contained mRNA encoding the DcR1 decoy receptor and only
macrophages contained DcR2 decoy receptor transcripts. DR4 mRNA was
present only in THP-1 cells and was the only ***TRAIL*** - ***R*** transcript increased by IFN-gamma. Cytotoxicity assays revealed that the
two trophoblast cell lines were resistant, whereas the two macrophage
lines were partially susceptible to killing by rTRAIL. Collectively, the
results are consistent with a role for the TRAIL/ ***TRAIL*** - ***R*** system in the establishment of placental immune privilege.

L2 ANSWER 29 OF 41 MEDLINE
DUPLICATE 10
ACCESSION NUMBER: 1999290669 MEDLINE
DOCUMENT NUMBER: 99290669 PubMed ID: 10364001
TITLE: Relation of TNF-related apoptosis-inducing ligand (TRAIL)
receptor and FLICE-inhibitory protein expression to
TRAIL-induced apoptosis of melanoma.
AUTHOR: Zhang X D; Franco A; Myers K; Gray C; Nguyen T; Hersey P
CORPORATE SOURCE: Immunology and Oncology Unit, Department of Surgical
Sciences, Newcastle, NSW, Australia.
SOURCE: CANCER RESEARCH, (1999 Jun 1) 59 (11) 2747-53.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 19990714
Entered Medline: 19990629
AB Past studies have shown that apoptosis mediated by TNF-related
apoptosis-inducing ligand (TRAIL) is regulated by the expression of two
death receptors [TRAIL receptor 1 (TRAIL-R1) and TRAIL-R2] and two decoy
receptors (TRAIL-R3 and TRAIL-R4) that inhibit apoptosis. In previous
studies, we have shown that TRAIL but not other members of the tumor
necrosis factor family induce apoptosis in approximately two-thirds of
melanoma cell lines. Here, we examined whether the expression of
TRAIL - ***R*** at the mRNA and protein level in a panel of 28
melanoma cell lines and melanocytes correlated with their sensitivity to
TRAIL-induced apoptosis. We report that at least three factors appear to
underlie the variability in TRAIL-induced apoptosis. (a) Four of nine cell
lines that were insensitive to TRAIL-induced apoptosis failed to express
death receptors, and in two instances, lines were devoid of all TRAIL-Rs.
Southern analysis suggested this was due to loss of the genes for the
death receptors. (b) Despite the presence of mRNA for the ***TRAIL*** -
R , some of the lines failed to express ***TRAIL*** - ***R*** protein on their surface. This was evident for TRAIL-R1 and more so for
the TRAIL decoy receptors TRAIL-R3 and -R4. Studies on permeabilized cells
revealed that the receptors were located within the cytoplasm and
redistribution from the cytoplasm may represent a posttranslational
control mechanism. (c) Surface expression of TRAIL-R1 and -R2 (but not
TRAIL-R3 and -R4) showed an overall correlation with TRAIL-induced
apoptosis. However, certain melanoma cell lines and clones were relatively
resistant to TRAIL-induced apoptosis despite the absence of decoy
receptors and moderate levels of TRAIL-R1 and -R2 expression. This may
indicate the presence of inhibitors within the cells, but resistance to
apoptosis could not be correlated with expression of the caspase inhibitor
FLICE-inhibitory protein. mRNA for another TRAIL receptor,
osteoprotegerin, was expressed in 22 of the melanoma lines but not on
melanocytes. Its role in induction of apoptosis remains to be studied.
These results appear to have important implications for future clinical
studies on TRAIL.

L2 ANSWER 30 OF 41 MEDLINE
DUPLICATE 11
ACCESSION NUMBER: 1999323989 MEDLINE
DOCUMENT NUMBER: 99323989 PubMed ID: 10395688
TITLE: IFN-gamma mediates a novel antiviral activity through
dynamic modulation of TRAIL and TRAIL receptor expression.
AUTHOR: Sedger L M; Shows D M; Blanton R A; Peschon J J; Goodwin R
G; Cosman D; Wiley S R
CORPORATE SOURCE: Department of Molecular Immunology, Immunex Corporation,
Seattle, WA 98101, USA.. sedger1@immunex.com
SOURCE: JOURNAL OF IMMUNOLOGY, (1999 Jul 15) 163 (2) 920-6.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 19990806
Entered Medline: 19990729
AB TNF-related apoptosis-inducing ligand (TRAIL) is able to kill many
transformed cells of diverse tissue types. We show that TRAIL is inducible
by IFN-gamma, by TNF-alpha, and by infection with human CMV, and has
potent antiviral activity in vitro. CMV infection and IFN-gamma also
reciprocally modulate TRAIL receptor (***TRAIL*** - ***R***)
expression. CMV infection increased the expression of TRAIL-R1 and -R2,
whereas IFN-gamma down-regulated the expression of TRAIL-Rs on uninfected
fibroblasts. Moreover, IFN-gamma significantly decreased the basal level
of NF-kappaB activation, a known survival factor that inhibits apoptosis.
Thus, TRAIL selectively kills virus-infected cells while leaving
uninfected cells intact, and IFN-gamma potentiates these effects by
dynamic modulation of TRAIL and ***TRAIL*** - ***R*** expression and
by sensitizing cells to apoptosis. The regulation of TRAIL and
TRAIL - ***R*** expression may represent a general mechanism
that contributes to the control of TRAIL-mediated apoptosis.

L2 ANSWER 31 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:263918 BIOSIS
DOCUMENT NUMBER: PREV199900263918
TITLE: To die or not to die-The quest of the TRAIL receptors.
AUTHOR(S): Degli-Esposti, Mariapia (1)
CORPORATE SOURCE: (1) Department of Microbiology, University of Western
Australia, QEII Medical Centre, L Block. corner Hampden Rd.
and Monash Ave., Nedlands, Perth, WA, 6009 Australia
SOURCE: Journal of Leukocyte Biology, (May, 1999) Vol. 65, No. 5,
pp. 535-542.
ISSN: 0741-5400.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The last 18 months have witnessed the characterization of several new
members of the tumor necrosis factor (TNF) receptor family. Among these
are five receptors for the cytotoxic ligand TRAIL (TNF-related
apoptosis-inducing ligand). Two of these receptors, TRAIL-R1 and TRAIL-R2,
contain classical cytoplasmic death domains and are able to transduce an
apoptotic signal. The others lack functional death domains and are not
able to promote cell death. Indeed, one of the receptors for TRAIL,
osteoprotegerin (OPG) is a soluble protein whose activities so far have
been shown to be inhibition of osteoclastogenesis and increased bone
density in vivo. The existence of multiple receptors for TRAIL suggests an
unexpected complexity to TRAIL-mediated biological functions.

L2 ANSWER 32 OF 41 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD DUPLICATE 12
ACCESSION NUMBER: 1998-480767 [41] WPIDS
DOC. NO. CPI: C1998-145392
TITLE: New TRAIL receptor protein and related oligomers, nucleic
acid, vectors - used to inhibit TRAIL activity, e.g. in
cases of thrombocytic purpura, clotting in small blood
vessels etc., also for diagnosis.
DERWENT CLASS: B04 D16
INVENTOR(S): RAUCH, C; WALCZAK, H
PATENT ASSIGNEE(S): (IMMV) IMMUNEX CORP
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9835986	A1	19980820	(199841)*	EN	56

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA IL JP KR MX NO NZ
AU 9866505 A 19980908 (199904)
EP 1005488 A1 20000607 (200032) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
US 6072047 A 20000606 (200033)
NZ 336929 A 20001124 (200065)
MX 9907234 A1 20000101 (200115)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9835986	A1	WO 1998-US2239	19980211
AU 9866505	A	AU 1998-66505	19980211
EP 1005488	A1	EP 1998-908474	19980211
		WO 1998-US2239	19980211
US 6072047	A CIP of	US 1997-799861	19970213
	CIP of	US 1997-815255	19970312
	CIP of	US 1997-829536	19970328
	CIP of	US 1997-869852	19970604
		US 1997-883036	19970626
NZ 336929	A	NZ 1998-336929	19980211
		WO 1998-US2239	19980211
MX 9907234	A1	MX 1999-7234	19990805

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9866505	A Based on	WO 9835986
EP 1005488	A1 Based on	WO 9835986
NZ 336929	A Based on	WO 9835986

PRIORITY APPLN. INFO: US 1997-883036 19970626; US 1997-799861
19970213; US 1997-815255 19970312; US 1997-829536 19970328; US 1997-869852 19970604
AN 1998-480767 [41] WPIDS
AB WO 9835986 A UPAB: 19981014
Purified TRAIL-receptor polypeptide (***TRAIL*** - ***R*** ; TRAIL =
tumour necrosis factor-related apoptosis-inducing ligand) that can bind
TRAIL and includes the sequence VPANEGD.
Also new are:
(1) oligomers containing 2-4 ***TRAIL*** - ***R*** molecules;
(2) isolated ***TRAIL*** - ***R*** DNA (I), its fragments and
DNA or RNA complements;
(3) expression vectors containing (I);
(4) host cells containing this vector, and
(5) antibodies (Ab) against ***TRAIL*** - ***R*** , and its
antigen-binding fragments.
USE - ***TRAIL*** - ***R*** is used:
(i) to purify or inhibit activity of TRAIL, in vitro or in vivo,
particularly its apoptosis-inducing action;
(ii) to measure amounts of TRAIL;
(iii) to identify TRAIL-expressing cells;
(iv) as carrier for therapeutic or diagnostic agents to such cells;
(v) as reagents for study effects of inhibiting TRAIL/ ***TRAIL*** - ***R*** interactions.
TRAIL - ***R*** , or its nucleic acid, can be

Fas/Apo1-mediated activation of JNK was unaffected by the expression of
GFP-DeltaFADD, suggesting that in Fas/Apo1 signaling the apoptotic pathway
and the activation of JNK diverge at a level proximal to the receptor,
upstream of or parallel to FADD.

L2 ANSWER 36 OF 41 MEDLINE
DUPLICATE 15
ACCESSION NUMBER: 1998211672 MEDLINE
DOCUMENT NUMBER: 98211672 PubMed ID: 9551946
TITLE: Lymphocyte inhibitor of TRAIL (TNF-related apoptosis-inducing ligand): a new receptor protecting
lymphocytes from the death ligand TRAIL.
AUTHOR: Mongkolsapaya J; Cowper A E; Xu X N; Morris G; McMichael A
J; Bell J I; Screaton G R
CORPORATE SOURCE: Molecular Immunology Group, Institute of Molecular
Medicine, John Radcliffe Hospital, Oxford, United Kingdom.
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Jan 1) 160 (1) 3-6.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: GENBANK-AF033845
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980507
AB Apoptosis can be triggered by the engagement of cell surface receptors by
their ligands. A growing number of receptors belonging to the TNF receptor
family have been identified that contain a conserved cytoplasmic death
domain. These include Fas, TNF-R1, lymphocyte-associated receptor of death
(LARD), DR4, and ***TNF*** - ***related*** ***apoptosis*** -
inducing ***ligand*** ***receptor*** inducer of cell
killing-2 (TRICK2). The latter two are receptors for the cytotoxic ligand
TNF-related apoptosis-inducing ligand (TRAIL), and one of the paradoxes
raised by the cloning of these molecules was why do most cells not die
upon contact with the widely expressed TRAIL molecule? This is a
particular problem for lymphocytes that express DR4 and TRICK2 and are in
constant circulation through TRAIL-expressing tissues. We have cloned LIT
(lymphocyte inhibitor of TRAIL), which lacks a death domain. LIT is
expressed predominantly on PBL, where it can competitively inhibit
TRAIL-induced apoptosis through DR4/TRICK2, and may function to modulate
lymphocyte sensitivity to TRAIL.

L2 ANSWER 37 OF 41 MEDLINE
DUPLICATE 16
ACCESSION NUMBER: 97431692 MEDLINE
DOCUMENT NUMBER: 97431692 PubMed ID: 9285725
TITLE: TRICK2, a new alternatively spliced receptor that
transduces the cytotoxic signal from TRAIL.
AUTHOR: Screaton G R; Mongkolsapaya J; Xu X N; Cowper A E;
McMichael A J; Bell J I
CORPORATE SOURCE: Molecular Immunology Group Institute of Molecular Medicine
John Radcliffe Hospital Oxford, OX3 9DS, UK.
SOURCE: CURRENT BIOLOGY, (1997 Sep 1) 7 (9) 693-6.
Journal code: B44; 9107782. ISSN: 0960-9822.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF018657; GENBANK-AF018658
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19990129
Entered Medline: 19980203
AB A subset of the tumour necrosis factor (TNF) receptor family contain a
conserved intracellular motif, the death domain. Engagement of these
receptors by their respective ligands initiates a signalling cascade that
rapidly leads to cell death by apoptosis. We have cloned a new member of
this family, TRICK2, the TRAIL (***TNF*** - ***related***
apoptosis - ***inducing*** ***ligand***) ***receptor***
inducer of cell killing 2. TRICK2 is expressed in a number of cell types,
and to particularly high levels in lymphocytes and spleen. Two isoforms of
the TRICK2 mRNA are generated by alternative pre-mRNA splicing and differ
by a 29 amino-acid extension to the extracellular domain. Overexpression
of TRICK2 rapidly induced apoptosis in 293T cells; this induction was
dependent upon the presence of the death domain of TRICK2. Using a soluble
molecule containing the TRICK2 extracellular domain, we demonstrated that
TRICK2, like DR4 [1], is a receptor for TRAIL/APO-2L [2,3] and could
inhibit TRAIL-induced killing of lymphocyte lines, such as the Jurkat
T-cell line. TRAIL is upregulated upon lymphocyte activation, as is the
intensively studied ligand for Fas, FasL [4]. TRAIL and its receptors
might therefore provide another system for the regulation of lymphocyte
selection and proliferation, as well as providing an additional weapon in
the armoury of cytotoxic lymphocytes.

L2 ANSWER 38 OF 41 MEDLINE
DUPLICATE 17
ACCESSION NUMBER: 97242415 MEDLINE
DOCUMENT NUMBER: 97242415 PubMed ID: 9087414
TITLE: Viral FLICE-inhibitory proteins (FLIPs) prevent apoptosis
induced by death receptors.
AUTHOR: Thome M; Schneider P; Hofmann K; Fickenscher H; Meinl E;
Neipel F; Mattmann C; Burns K; Bodmer J L; Schroter M;
Scaffidi C; Krammer P H; Peter M E; Tschopp J
CORPORATE SOURCE: Institute of Biochemistry, University of Lausanne,
Epalinges, Switzerland.
SOURCE: NATURE, (1997 Apr 3) 386 (6624) 517-21.
Journal code: NSC; 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U93872
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 20000303
Entered Medline: 19970428
AB Viruses have evolved many distinct strategies to avoid the host's
apoptotic response. Here we describe a new family of viral inhibitors
(v-FLIPs) which interfere with apoptosis signalled through death receptors
and which are present in several gamma-herpesviruses (including
Kaposi's-sarcoma-associated human herpesvirus-8), as well as in the
tumorigenic human molluscipoxvirus. v-FLIPs contain two death-effector
domains which interact with the adaptor protein FADD, and this inhibits
the recruitment and activation of the protease FLICE by the CD95 death
receptor. Cells expressing v-FLIPs are protected against apoptosis induced
by CD95 or by the related death receptors TRAMP and ***TRAIL*** -
R . The herpesvirus saimiri FLIP is detected late during the lytic
viral replication cycle, at a time when host cells are partially protected
from CD95-ligand-mediated apoptosis. Protection of virus-infected cells
against death-receptor-induced apoptosis may lead to higher virus
production and contribute to the persistence and oncogenicity of several
FLIP-encoding viruses.

L2 ANSWER 39 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:79792 SCISEARCH
THE GENUINE ARTICLE: YR236
TITLE: Dominant-negative FADD inhibits TNFR60-, Fas/Apo1- and
TRAIL - ***R*** /Apo2-mediated cell death but not
gene induction
AUTHOR: Wajant H (Reprint); Johannes F J; Haas E; Siemienski K;
Schwenzer R; Schubert G; Weiss T; Grell M; Scheurich P
CORPORATE SOURCE: UNIV STUTTGART, INST CELL BIOL & IMMUNOL, ALLMANDRING 31,
D-70569 STUTTGART, GERMANY (Reprint)
COUNTRY OF AUTHOR: GERMANY
SOURCE: CURRENT BIOLOGY, (15 JAN 1997) Vol. 8, No. 2, pp. 113-116.
Publisher: CURRENT BIOLOGY LTD, 34-42 CLEVELAND STREET,
LONDON, ENGLAND W1P 6LB.
ISSN: 0960-9822.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 27
"ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS"
AB Fas/Apo1 and other cytotoxic receptors of the tumor necrosis factor
receptor (TNFR) family contain a cytoplasmic death domain (Db) [1-11] that
activates the apoptotic process by interacting with the DD-containing
adaptor proteins TNFR-associated Db protein (TRADD) [12,13] and
pas-associated DD protein (FADD/MORT1) [14,15], leading to the activation
of cysteine proteases of the caspase family [16], Stimulation of Fas/Apo1
reads to the formation of a receptor-bound death-inducing signaling
complex (DISC), consisting of FADD and two different forms of caspase-8
[17-19]. Transient expression of a dominant-negative mutant of FADD
impairs TNFR60-mediated and Fas/Apo1-mediated apoptosis [13,20], but has
no effect on TNF-related apoptosis-inducing ligand (TRAIL/Apo2L)-induced
cell death [7-10,21], To study the function of FADD in DD-receptor
signaling in more detail, we established HeLa cells that stably expressed
a green fluorescent protein (GFP)-tagged dominant-negative mutant of FADD,
GFP-Delta FADD. Interestingly, expression of this mutant inhibited cell
death induced by TNFR60, Fas/Apo1 and ***TRAIL*** - ***R*** /Apo2. In
addition, GFP-Delta FADD did not interfere with TNF-mediated gene
induction or with activation of NF-kappa B or Jun N-terminal kinase (JNK),
demonstrating that FADD is part of the TNFR60-initiated apoptotic pathway
but does not play a role in TNFR60-mediated gene induction.
Fas/Apo1-mediated activation of JNK was unaffected by the expression of
GFP-Delta FADD, suggesting that in Fas/Apo1 signaling the apoptotic
pathway and the activation of JNK diverge at a level proximal to the
receptor, upstream of or parallel to FADD.

L2 ANSWER 40 OF 41 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1988:70537 BIOSIS
DOCUMENT NUMBER: BA85:36836
TITLE: MEASUREMENT OF THE GRISTLE CONTENT IN BEEF BY MACROSCOPIC
UV FLUOROMETRY.
AUTHOR(S): SWATLAND H J
CORPORATE SOURCE: DEP. FOOD SCI., UNIV. GUELPH, GUELPH, ONTARIO, CAN.
SOURCE: J ANIM SCI, (1987) 65 (1), 158-164.
CODEN: JANSAG. ISSN: 0021-8812.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Ultraviolet light (365 nm) was directed at an angle of 45.degree. onto
meat samples in a circular aperture (3 cm diameter). Fluorescence
emissions were measured with a monochromator and a photomultiplier tube.
Intact tendons and elastic ligaments had a strong fluorescence emission
peak around 440 to 450 nm and only weak fluorescence around 510 nm.
Tissues such as lean meat and adipose tissue that contain a matrix of
reticular fibers (Type III collagen) had very low fluorescence around 440
to 450 nm so that their peak emittance was the weak fluorescence peak at
510 nm. The 510/440 nm ratio of fluorescence emissions was measured in

used to
treat conditions involving defective or inadequate ***TRAIL*** - ***R*** , e.g. thrombotic thrombocytopaenic purpura, haemolytic-uraemic
syndrome, clotting of small blood vessels, systemic lupus erythematosus
and TRAIL-mediated apoptosis of T cells in human immune deficiency virus
infections.
Ab are used for detection or purification of ***TRAIL*** - ***R*** , and to inhibit TRAIL/ ***TRAIL*** - ***R*** interaction,
i.e. to treat the above diseases; also agonist antibodies can be used to
induce apoptosis in some cancer or virus-infected cells.
(I) can be used to detect abnormal ***TRAIL*** - ***R*** genes
and as antisense therapeutics.
TRAIL - ***R*** may be administered in soluble form or it
is immobilised on a solid support and used for extracorporeal treatment of
blood.
Dwg.0/3

L2 ANSWER 33 OF 41 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-399141 [34] WPIDS
CROSS REFERENCE: 1998-399142 [34]
DOC. NO. CPI: C1998-120982
TITLE: Human TRAIL receptor without an intracellular domain
polypeptide - used in the diagnosis of immune system-related disorder(s).
DERWENT CLASS: B04 D16
INVENTOR(S): EBNER, R; FENG, P; GENTZ, R L; NI, J; RUBEN, S M; WEI, Y;
YU, G
PATENT ASSIGNEE(S): (HUMA-N) HUMAN GENOME SCI INC
COUNTRY COUNT: 82
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9830693	A2	19980716 (199834)*		EN	91

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA
PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
US UZ VN YU ZW
AU 9862386 A 19980803 (199850)
EP 990031 A2 20000405 (200021) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1247567 A 20000315 (200031)
JP 2001505060 W 20010417 (200128) 150

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9830693	A2	WO 1998-US152	19980113
AU 9862386	A	AU 1998-62386	19980113
EP 990031	A2	EP 1998-904528	19980113
		WO 1998-US152	19980113
CN 1247567	A	CN 1998-801836	19980113
JP 2001505060 W		JP 1998-531036	19980113
		WO 1998-US152	19980113

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9862386	A Based on	WO 9830693
EP 990031	A2 Based on	WO 9830693
JP 2001505060 W	Based on	WO 9830693

PRIORITY APPLN. INFO: US 1997-54885 19970807; US 1997-35496 19970114
AN 1998-399141 [34] WPIDS
CR 1998-399142 [34]
AB WO 9830693 A UPAB: 20010522
Isolated nucleic acid molecule (I) comprises a sequence at least 95 %
identical to: (a) a nucleotide sequence encoding a mature or immature TRID
(TRAIL (***TNF*** - ***related*** ***apoptosis*** - ***inducing*** ***ligand***) ***receptor*** without an
intracellular domain) polypeptide having a 259 amino acid (aa) sequence
(A) (includes 26 aa signal peptide) given in the specification or the
mature or immature TRID polypeptide encoded by ATCC 97798; (b) a
nucleotide sequence encoding the soluble extracellular domain of a TRID
polypeptide comprising aa 27-240 of (A) or the soluble extracellular
domain of the TRID polypeptide encoded by ATCC 97798; and (c) a nucleotide
sequence complementary to any of the nucleotide sequences of (a) and (b).
Also claimed are: (1) an isolated nucleic acid comprising a
nucleotide sequence at least 95 % identical to a sequence encoding
residues m-233, 1-x or m-x of the 259 aa sequence; m= -1 to 27 and x=
123-233; (2) an isolated nucleic acid comprising a nucleotide sequence at
least 95% identical to: (a) a sequence encoding the TRID protein encoded
by ATCC 97798 having an N-terminal truncation of 1-52 aa; and/or (b) a
sequence encoding the TRID protein encoded by ATCC 97798 having a
C-terminal truncation of 1-110 aa; (3) an isolated nucleic acid comprising
a polynucleotide which encodes an epitope bearing portion of a TRID
polypeptide encoded by (I); (4) a recombinant vector containing (I); (5) a
recombinant host cell comprising the vector of (4); (6) a TRID polypeptide
(A) encoded by (I); and (7) an antibody that binds specifically to (A).
USE - TRID is a member of the tumour necrosis factor receptor (TNFR)
family also known as TNFR-5. TRID is expressed in haematopoietic tissues
and other normal human tissues. For a number of immune system-related
disorders, substantially altered (whether increased or decreased) levels
of TRID gene expression can be detected, therefore the TRID polypeptides,
nucleic acids and antibodies are useful in the diagnosis of such immune
system related disorders. Mutations of the TRID gene can also be detected.
TRID can also be used to identify ligands which may be useful in the
treatment of apoptosis related disorders. TRID is administered to humans
at a parenteral dose of 0.01 to 1 mg/kg/day.
Dwg.0/10

L2 ANSWER 34 OF 41 MEDLINE
DUPLICATE 13
ACCESSION NUMBER: 1998414313 MEDLINE
DOCUMENT NUMBER: 98414313 PubMed ID: 9743381
TITLE: TNFR80-dependent enhancement of TNFR60-induced cell death
is mediated by TNFR-associated factor 2 and is specific for
TNFR60.
AUTHOR: Weiss T; Grell M; Siemienski K; Muhlenbeck F; Durkop H;
Pfizenmaier K; Scheurich P; Wajant H
CORPORATE SOURCE: Institute of Cell Biology and Immunology, University of
Stuttgart, Germany.
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Sep 15) 161 (6) 3136-42.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981020
Last Updated on STN: 19981020
Entered Medline: 19981006
AB Costimulation of TNFR80 can strongly enhance TNFR60-induced cell death. In
this study, we show that this enhancement is TNFR60 selective, as neither
TNF-related apoptosis-inducing ligand/Apo2 ligand-, Apo1/Fas-, ceramide-,
nor daunorubicin-mediated cell death was affected by costimulation of
TNFR80. We further demonstrate that TNFR-associated factor 2 (TRAF2) is
critically involved in both negative and positive regulation of TNF-induced cell death. Overexpression of TRAF2 and of a TRAF2 mutant,
deficient in nuclear factor-kappaB activation, selectively desensitized
and enhanced, respectively, TNFR60-induced cell death in HeLa cells.
However, upon costimulation of TNFR80, which mediates activation of
nuclear factor-kappaB and the c-Jun amino-terminal kinase via TRAF2,
TNF-induced cell death is drastically enhanced in parental and
TRAF2-transfected, but not in TRAF2 (87-501)-transfected cells. These data
point to a critical role of TRAF2 in the apoptotic TNFR cross talk,
whereby the TNFR80-dependent enhancement of TNFR60-induced cell death is
due to TNFR80-mediated negative regulation of TRAF2 function(s). An
interference with TRAF2 function was confirmed independently by analysis
of c-Jun amino-terminal kinase activation via TNFR60 upon prestimulation
of TNFR80. We propose that the apoptotic TNFR cross talk is based on
TNFR80-mediated abrogation of antiapoptotic TRAF2-dependent signaling
pathways initiated by TNFR60, but not Apo1/Fas or the apoptotic
TNF - ***related*** ***apoptosis*** - ***inducing*** ***ligand*** ***receptors*** .

L2 ANSWER 35 OF 41 MEDLINE
DUPLICATE 14
ACCESSION NUMBER: 1998089174 MEDLINE
DOCUMENT NUMBER: 98089174 PubMed ID: 9427646
TITLE: Dominant-negative FADD inhibits TNFR60-, Fas/Apo1- and
TRAIL - ***R*** /Apo2-mediated cell death but not
gene induction.
AUTHOR: Wajant H; Johannes F J; Haas E; Siemienski K; Schwenzer R;
Schubert G; Weiss T; Grell M; Scheurich P
CORPORATE SOURCE: Institute of Cell Biology and Immunology, University of
Stuttgart, Allmandring 31, 70569 Stuttgart, Germany..
harald.wajant@po.uni-stuttgart.de
SOURCE: CURRENT BIOLOGY, (1998 Jan 15) 8 (2) 113-6.
Journal code: B44; 9107782. ISSN: 0960-9822.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980326
Last Updated on STN: 19980326
Entered Medline: 19980318
AB Fas/Apo1 and other cytotoxic receptors of the tumor necrosis factor
receptor (TNFR) family contain a cytoplasmic death domain (DD) [1] [2] [3]
[4] [5] [6] [7] [8] [9] [10] [11] that activates the apoptotic process by
interacting with the DD-containing adaptor proteins TNFR-associated DD
protein (TRADD) [12] [13] and Fas-associated DD protein (FADD/MORT1) [14]
[15], leading to the activation of cysteine proteases of the caspase
family [16]. Stimulation of Fas/Apo1 leads to the formation of a
receptor-bound death-inducing signaling complex (DISC), consisting of FADD
and two different forms of caspase-8 [17] [18] [19]. Transient expression
of a dominant-negative mutant of FADD impairs TNFR60-mediated and
Fas/Apo1-mediated apoptosis [13] [20], but has no effect on TNF-related
apoptosis-inducing ligand (TRAIL/Apo2L)-induced cell death [7] [8] [9]
[10] [21]. To study the function of FADD in DD-receptor signaling in more
detail, we established HeLa cells that stably expressed a green
fluorescent protein (GFP)-tagged dominant-negative mutant of FADD,
GFP-DeltaFADD. Interestingly, expression of this mutant inhibited cell
death induced by TNFR60, Fas/Apo1 and ***TRAIL*** - ***R*** /Apo2. In
addition, GFP-DeltaFADD did not interfere with TNF-mediated gene induction
or with activation of NF-kappaB or Jun N-terminal kinase (JNK),
demonstrating that FADD is part of the TNFR60-initiated apoptotic pathway
but does not play a role in TNFR60-mediated gene induction.

comminuted meat samples containing varying mixtures of lean meat and
gristle and varying mixtures of muscles with a high and low gristle
content. The 510/440 nm ratio was correlated with the ratio of lean
meat/gristle (r = .96, P < .005). The 510/440 nm ratio was correlated with
the ratio of longissimus/shank meat (two ***trails*** ; ***r*** =
.93, P < .01; and r = .94, P < .005). Results were only slightly changed
when samples had dry surfaces or when samples were mixed with adipose
particles. The relationship between the area of gristle in the samples and
the 510/440 nm ratio was curvilinear with the greatest sensitivity to the
fewest gristle fragments.

L2 ANSWER 41 OF 41 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1974-17418V [39] WPIDS
TITLE: Hydraulic brake system for ***trail*** ***r*** .
has distributor valv responsive to mechanical brake of
towing vehicle.
DERWENT CLASS: Q18
PATENT ASSIGNEE(S): (BOSC) BOSCH GMBH ROBERT
COUNTRY COUNT: 4
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 3836205	A	19740917	(197439)*		
GB 1379373	A	19750102	(197501)		
AT 7304222	A	19760715	(197632)		
DE 2225357	B	19810326	(198114)		

PRIORITY APPLN. INFO: DE 1972-2225357 19720525
**** DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER